Exhibit B

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WHO Infection Control Guidelines for Transmissible Spongiform Encephalopathies

Report of a WHO consultation
Geneva, Switzerland, 23-26 March 1999

World Health Organization
Communicable Disease Surveillance and Control

5.4 Transport of specimens by air

The transportation of pathology samples by air must comply with the International Air Transport Association (IATA) Restricted Articles Regulations and any additional requirements of the individual carriers. Documentation required by the IATA includes Shipper's Certificate for Restricted Articles, which requires that the content, nature and quantity of infectious material to be disclosed. The WHO Guidelines for the Safe Transport of Infectious Substances and Diagnostic Specimens[16] provides more information on the safe transport of material. Where properly packaged according to these guidelines, there is no danger to the carriers.

Section 6. DECONTAMINATION PROCEDURES

6.1 General considerations

TSE agents are unusually resistant to disinfection and sterilization by most of the physical and chemical methods in common use for decontamination of infectious pathogens. Table 8 lists a number of commonly used chemicals and processes that cannot be depended upon for decontamination, as they have been shown to be either ineffective or only partially effective in destroying TSE infectivity. Variability in the effectiveness appears to be highly influenced by the nature and physical state of the infected tissues. For example, infectivity is strongly stabilized by drying or fixation with alcohol, formalin or glutaraldehyde. As a consequence, contaminated materials should not be exposed to fixation reagents, and should be kept wet between the time of use and disinfection by immersion in chemical disinfectants.

Table 8 Ineffective or sub-optimal disinfectants

Chemical disinfectants	Gaseous disinfectants	Physical processes
Ineffective[17]	Ineffective	Ineffective
alcohol	ethylene oxide	boiling
ammonia	formaldehyde	dry heat (<300°C)
ß-propiolactone		ionising, UV or microwave radiation
formalin		
hydrochloric acid		
hydrogen peroxide		
peracetic acid		
phenolics		
sodium dodecyl sulfate (SDS) (5%)		
Variably or partially effective		Variably or partially effective
chlorine dioxide		autoclaving at 121°C for 15 minutes
glutaraldehyde		boiling in 3% sodium dodecyl
guanidinium thiocyanate (4 M)		sulfate (SDS)
iodophores		
sodium dichloro-isocyanurate		
sodium metaperiodate		
urea (6 M)		

[16] Guidelines for the Safe Transport of Infectious Substances and Diagnostic Specimens. Geneva, World Health Organization, 1997. WHO/EMC/97.3.

[17] Some of these chemicals may have very small effects on TSE infectivity and are not adequate for disinfection.

6.2 Decontamination of instruments

Policy makers should be guided by the infectivity level of the tissue contaminating the instrument and by the expectations of how the instrument will be re-used, as per Section 2.4. In this way, the most stringent recommendations are applied to instruments contacting high infectivity tissues of a person with a known TSE, which will also subsequently be re-used in the CNS or spinal column. Policy makers are encouraged to adopt the highest decontamination methods feasible until studies are published which clarify the risk of re-using decontaminated instruments.

Annex III lists the decontamination methods recommended by the consultation in order of decreasing effectiveness. It was emphasized that the safest and most unambiguous method for ensuring that there is no risk of residual infectivity on surgical instruments is to discard and destroy them by incineration. While this strategy should be universally applied to those devices and materials that are designed to be disposable, it was also recognized that this may not be feasible for many devices and materials that were not designed for single use. For these situations, the methods recommended in Annex III appear to remove most and possibly all infectivity under the widest range of conditions.

Those surgical instruments that are going to be re-used may be mechanically cleaned in advance of subjecting them to decontamination. Mechanical cleaning will reduce the bio-load and protect the instrument from damage caused by adherent tissues. If instruments are cleaned before decontamination, the cleaning materials must be treated as infectious waste, and the cleaning station must be decontaminated by one of the methods listed in Annex III. The instruments are then treated by one of the decontamination methods recommended in Annex III before reintroduction into the general instrument sterilization processes. A minority opinion held that instruments should be decontaminated before mechanical cleaning, and then handled as per general instrument sterilization processes.

Annex III recommends that, where possible, two or more different methods of inactivation be combined in any sterilization procedure for these agents. Procedures that employ heat and NaOH (either consecutively or simultaneously) appear to be sterilizing under worst-case conditions (e.g., infected brain tissue partly dried on to surfaces). Moreover, hot alkaline hydrolysis reduces biological macromolecules to their constituent sub-units, thereby cleaning as well as inactivating.

The consultation recognized that complex and expensive instruments such as intracardiac monitoring devices, fiberoptic endoscopes, and microscopes cannot be decontaminated by the harsh procedures specified in Annex III. Instead, to the extent possible, such instruments should be protected from surface contamination by wrapping or bagging with disposable materials. Those parts of the device that come into contact with internal tissues of patients should be subjected to the most effective decontaminating procedure that can be tolerated by the instrument. All adherent material must be removed and, if at all possible, the exposed surfaces cleaned using a decontamination method recommended in Annex III. Some instruments can be partly disassembled (e.g. drills and drill bits). Removable parts that would not be damaged by autoclaving, NaOH, or bleach should be dismounted and treated with these agents. In all instances where unfamiliar decontamination methods are attempted, the manufacturer should be consulted. These cleaning procedures should be applied even if the instrument has been re-used before discovery of its potential contamination.

Contaminated instruments or other contaminated materials should not be cleaned in automated washers without first having been decontaminated using a method recommended in Annex III.

6.3 Decontamination of work surfaces

Because TSE infectivity persists for long periods on work surfaces, it is important to use disposable cover sheets whenever possible to avoid environmental contamination, even though transmission to humans has never been recognized to have occurred from environmental exposure. It is also important to mechanically clean and disinfect equipment and surfaces that are subject to potential contamination, to prevent environmental build-ups. Surfaces contaminated by TSE agents can be disinfected by flooding, for one hour, with NaOH or sodium hypochlorite, followed by water rinses (see Annex III for detailed instructions). Surfaces that cannot be treated in this manner should be thoroughly cleaned; consider use of a partially effective method as listed in Table 8. Cleaning materials treated as potentially contaminated (see Section 6.4).

6.4 Decontamination of wastes and waste-contaminated materials

Decontamination of waste liquid and solid residues should be conducted with the same care and precautions recommended for any other exposure to TSE agents. The work area should be selected for easy containment of contamination and for subsequent disinfection of exposed surfaces. All waste liquids and solids must be captured and treated as infectious waste.

Liquids used for cleaning should be decontaminated in situ by addition of NaOH or hypochlorite or any of the procedures listed in Annex III, and may then be disposed of as routine hospital waste. Absorbents, such as sawdust, may be used to stabilize liquids that will be transported to an incinerator; however, this should be added after decontamination.

Cleaning tools and methods should be selected to minimize dispersal of the contamination by splashing, splatters and aerosols. Great care is required in the use of brushes and scouring tools. Where possible, cleaning tools such as brushes, towelling and scouring pads, as well as tools used for disassembling contaminated apparatus, should either be disposable or selected for their ability to withstand the disinfection procedures listed in Annex III.

Upon completion of the cleaning procedure, all solid wastes including disposable cleaning materials should be collected and decontaminated. Incineration is highly recommended. The cleaning station should then itself be decontaminated using one of the methods in Annex III.

Automated cleaning equipment must not be used for any instrument or material that has not previously been thoroughly decontaminated following the recommendations in Section 6.2 and Annex III.

6.5 Personal protection during decontamination procedures

Persons involved in the disinfection and decontamination of instruments or surfaces exposed to the tissues of persons with TSE should wear single-use protective clothing, gloves, mask and visor or goggles, as noted in Section 5.1, Table 6. The recommendations found in Table 6 can be adapted to different situations. All individuals involved with disinfection and decontamination procedures should be familiar with these basic protective measures and precautions. Handling of contaminated instruments during transfers and cleaning should be kept to a minimum.

Annex III Decontamination methods for Transmissible Spongiform Encephalopathies

The safest and most unambiguous method for ensuring that there is no risk of residual infectivity on contaminated instruments and other materials is to discard and destroy them by incineration. In some healthcare situations, as described in the guidance, one of the following less effective methods may be preferred. Wherever possible, instruments and other materials subject to re-use should be kept moist between the time of exposure to infectious materials and subsequent decontamination and cleaning. If it can be done safely, removal of adherent particles through mechanical cleaning will enhance the decontamination process.

The following recommendations are based on the best available evidence at this time and are listed in order of more to less severe treatments. These recommendations may require revision if new data become available.

1. Incineration

1. Use for all disposable instruments, materials, and wastes.
2. Preferred method for all instruments exposed to high infectivity tissues.

2. Autoclave/chemical methods for heat-resistant instruments

1. Immerse in sodium hydroxide (NaOH)[20] and heat in a gravity displacement autoclave at 121°C for 30 min; clean; rinse in water and subject to routine sterilization.
2. Immerse in NaOH or sodium hypochlorite[21] for 1 hr; transfer instruments to water; heat in a gravity displacement autoclave at 121°C for 1 hr; clean and subject to routine sterilization.
3. Immerse in NaOH or sodium hypochlorite for 1 hr.; remove and rinse in water, then transfer to open pan and heat in a gravity displacement (121°C) or porous load (134°C) autoclave for 1 hr.; clean and subject to routine sterilization.
4. Immerse in NaOH and boil for 10 min at atmospheric pressure; clean, rinse in water and subject to routine sterilization.
5. Immerse in sodium hypochlorite (preferred) or NaOH (alternative) at ambient temperature for 1 hr; clean; rinse in water and subject to routine sterilization.
6. Autoclave at 134°C for 18 minutes.[22]

[20] Unless otherwise noted, the recommended concentration is 1N NaOH.
[21] Unless otherwise noted, the recommended concentration is 20 000 ppm available chlorine.
[22] In worse-case scenarios (brain tissue bake-dried on to surfaces) infectivity will be largely but not completely removed.

3. Chemical methods for surfaces and heat sensitive instruments

1. Flood with 2N NaOH or undiluted sodium hypochlorite; let stand for 1 hr.; mop up and rinse with water.
2. Where surfaces cannot tolerate NaOH or hypochlorite, thorough cleaning will remove most infectivity by dilution and some additional benefit may be derived from the use of one or another of the partially effective methods listed in Section 5.1 (Table 8).

4. Autoclave/chemical methods for dry goods

1. Small dry goods that can withstand either NaOH or sodium hypochlorite should first be immersed in one or the other solution (as described above) and then heated in a porous load autoclave at $\geq$ 121°C for 1 hr.
2. Bulky dry goods or dry goods of any size that cannot withstand exposure to NaOH or sodium hypochlorite should be heated in a porous load autoclave at 134°C for 1 hr.

5. Notes about autoclaving and chemicals

Gravity displacement autoclaves: Air is displaced by steam through a port in the bottom of the chamber. Gravity displacement autoclaves are designed for general decontamination and sterilization of solutions and instruments.

Porous load autoclaves: Air is exhausted by vacuum and replaced by steam. Porous load autoclaves are optimized for sterilization of clean instruments, gowns, drapes, towelling, and other dry materials required for surgery. They are not suitable for liquid sterilization.

Sodium Hydroxide (NaOH, or soda lye): Be familiar with and observe safety guidelines for working with NaOH. 1N NaOH is a solution of 40 g NaOH in 1 litre of water. 1 N NaOH readily reacts with CO_2 in air to form carbonates that neutralize NaOH and diminish its disinfective properties. 10 N NaOH solutions do not absorb CO_2, therefore, 1N NaOH working solutions should be prepared fresh for each use either from solid NaOH pellets, or by dilution of 10 N NaOH stock solutions.

Sodium hypochlorite (NaOCl solution, or bleach): Be familiar with and observe safety guidelines for working with sodium hypochlorite. Household or industrial strength bleach is sold at different concentrations in different countries, so that a standard dilution cannot be specified. Efficacy depends upon the concentration of available chlorine and should be 20 000 ppm available chlorine. One common commercial formulation is 5.25% bleach, which contains 25 000 ppm chlorine. Therefore, undiluted commercial bleach can be safely used. If solid precursors of hypochloric acid is available, then stock solution and working solutions can be prepared fresh for each use.

6. Cautions regarding hazardous materials

In all cases, hazardous materials guidelines must be consulted.

1. Personnel

NaOH is caustic but relatively slow acting at room temperature, and can be removed from skin or clothing by thorough rinsing with water. Hot NaOH is aggressively caustic, and should not be handled until cool. The hazard posed by hot NaOH explains the need to limit boiling to 10 minutes, the shortest time known to be effective.
Hypochlorite solutions continuously evolve chlorine and so must be kept tightly sealed and away from light. The amount of chlorine released during inactivation may be sufficient to create a potential respiratory hazard unless the process is carried out in a well-ventilated or isolated location.

2. Material

In principle, NaOH does not corrode stainless steel, but in practice some formulations of stainless steel can be damaged (including some used for surgical instruments). It is advisable to test a sample or consult with the manufacturer before dedicating a large number of instruments to decontamination procedures. NaOH is known to be corrosive to glass and aluminum. Hypochlorite does not corrode glass or aluminum and has also been shown to be an effective sterilizing agent; it is, however, corrosive both to stainless steel and to autoclaves and (unlike NaOH) cannot be used as an instrument bath in the autoclave. If hypochlorite is used to clean or soak an instrument, it must be completely rinsed from the surfaces before autoclaving. Other decontamination methods may need testing, or consultation with the manufacturer to verify their effect on the instrument.